DHA Immunization Healthcare Division
COVID-19 Vaccine Safety Technical (VaST) Working Group

Myocarditis Following mRNA SARS-CoV-2 Vaccines

(b) (6) [redacted]
Defense Health Agency, Immunization Healthcare Division

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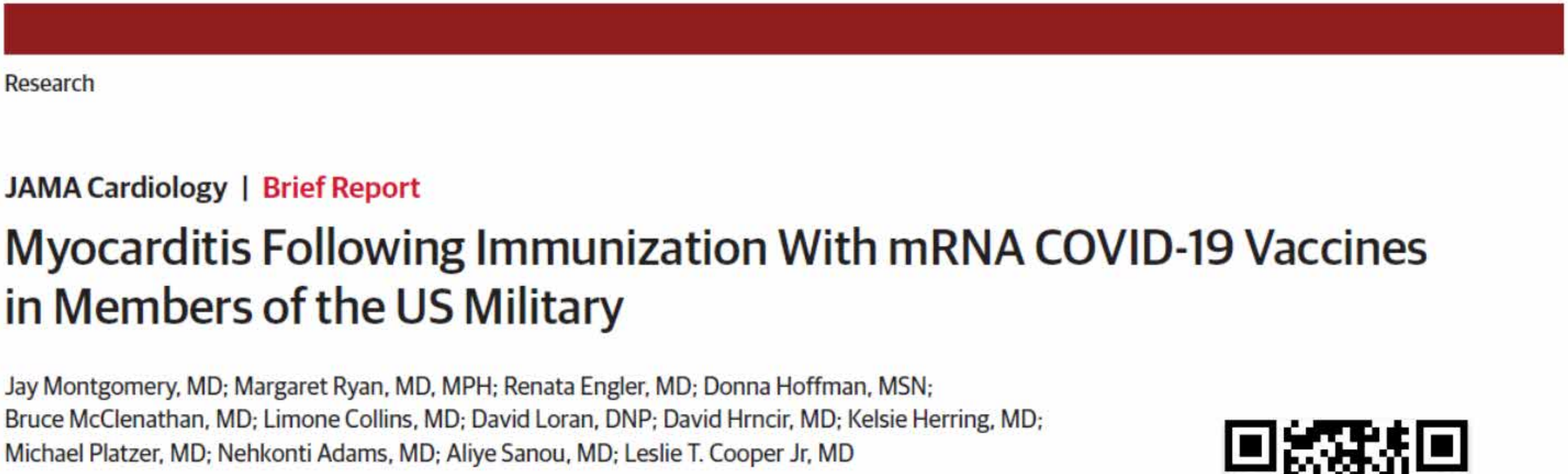
Objective

Provide update on myocarditis following COVID-19 vaccinations within the Military Health System

- 12 April VaST Briefing ([redacted] (b)(6)) 14 cases
- 17 May VaST Briefing ([redacted] (b)(6) 22 cases
- Introduce JAMA Cardiology paper (29 June) 23 cases
- Augment information previously shared with additional patient experience (43 cases)



Research

JAMA Cardiology | Brief Report

Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military

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Access at: https://jamanetwork.com/journals/jamacardiology/fullarticle/2781601

Past Cases Follow Up

- Of the 23 patients previously described, we reported 16 patients resolved their cardiac symptoms w/in 1-2 weeks of onset while 7 patients continued to have mild to moderate chest discomfort.
  - ☐ At 6 weeks post symptom onset, 5 (21%) remain symptomatic
    1. “short seconds of chest discomfort”; exercise EKG normal
    2. “occasional chest pain”; EKG normal, Holter normal, EST normal
    3. “chest pain occasionally”; EKG normal, ECHO normal
    4. “chest pain w/ exertion”; civilian cardiologist records requested
    5. “chest pain interrupts some physical activities”; stationed OCONUS with non-US cardiologist, 6-week follow-up pending
  - ☐ IAW AHA/ACC 2015 guidelines, all military members with myocarditis remain limited from strenuous activity for at least 3 months [1]
  - ☐ Eckart, et al., reported 13% atypical, non-limiting persistent chest discomfort following SPV-associated MPC [2]
  - ☐ Engler, et al., studying SPV-associated MPC outcomes report ~16% have unresolved prolonged clinical symptoms

1. J Am Coll Cardiol. 2015;66(21):2362–2371.
2. J Am Coll Cardiol. 2004 Jul 7;44(1):201-5.

Current Cases Update

- >50 individuals are being assessed for the onset of acute chest pain following COVID-19 vaccination since 21 Jan 2021. 43 evaluations completed
    - 39 diagnosed with myocarditis
    - 4 diagnosed with presumptive pericarditis
- Median onset of myocarditis = 48 hrs; pericarditis = 60 hrs
- Age:
    - Myocarditis: median 24 years (range 15-51)
    - Pericarditis: median 33 years (20-40)
- Sex:
    - Myocarditis: 35 male, 4 female
    - Pericarditis: 2 male, 2 female
- Race/ethnicity:
    - Myocarditis: 31 White, 3 Black, 5 other/unknown
    - Pericarditis: 1 White, 2 Black, 1 other/unknown

Current Cases Update

- Proximate vaccine doses:
  - ☐ Myocarditis
    - 21 cases presented after Moderna dose #2
    - 13 cases presented after Pfizer dose #2
    - 3 cases presented after Moderna dose #1*
    - 2 case presented after Pfizer dose #1*
    - 0 cases presented after Janssen vaccine
  - ☐ Pericarditis
    - 1 case presented after Moderna dose #2
    - 0 cases presented after Pfizer dose #2
    - 1 case presented after Moderna dose #1
    - 0 case presented after Pfizer dose #1
    - 2 cases presented after Janssen vaccine

** 3 had confirmed prior COVID-19 infection 2-4 months prior, 2 had no known infection history*

Current Cases Update

- Of the 39 myocarditis cases, all were considered probable or confirmed by the 2021 CDC Working Case Definition for Acute Myocarditis [1]
  - 79% (31) had abnormal ECGs (8 were normal)
  - 92% (36) had Troponin elevation (3 not done)
  - 90% (35) had normal echocardiogram (4 had mildly reduced LVEF (40%-50%))
  - 59% (23) underwent coronary artery imaging
    - 17 cardiac catheterization, 6 coronary computed tomography angiography
    - 100% (23) had normal exams
  - 16 underwent cMRI
    - 81% (13) had cMRI findings consistent with myocarditis
  - None had evidence of acute SARS-CoV-2 infection

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1. MMWR Morb Mortal Wkly Rep 2021;70:977–982. DOI: http://dx.doi.org/10.15585/mmwr.mm7027e2external icon

Expected-vs-Observed Myocarditis Cases

Assume observation window is 21 days following every vaccine dose

DoD administered vaccines (thru 30 Jun 2021)	**Expected* number myocarditis cases**	**Observed number myocarditis cases**
4,148,000 total doses of mRNA vaccine	2-24	39
1,851,000 2nd doses of mRNA vaccine	1-11	34
819,000 2nd doses of mRNA vaccine to military members	0-5	28
655,000 2nd doses of mRNA vaccine to male military members	0-4	27

* Assume expected rate of 1-10 cases per 100,000 person-years

Reference: Gubernot D, Jazwa A, Niu M, et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. *Vaccine*. 2021;39(28):3666-7

Expected-vs-Observed Myocarditis Cases

Assume observation window is 7 days following every vaccine dose

DoD administered vaccines (thru 30 Jun 2021)	**Expected* number myocarditis cases**	**Observed number myocarditis cases**
4,148,000 total doses of mRNA vaccine	1-8	38
1,851,000 2nd doses of mRNA vaccine	0-4	34
819,000 2nd doses of mRNA vaccine to military members	0-2	28
655,000 2nd doses of mRNA vaccine to male military members	0-1	27

* Assume expected rate of 1-10 cases per 100,000 person-years

Reference: Gubernot D, Jazwa A, Niu M, et al. U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines. *Vaccine*. 2021;39(28):3666-7

Summary

- Myocarditis appears to be a rare, but important, AEFI that is most frequently associated with 2nd dose of a mRNA COVID-19 vaccine in younger, mostly male, patients
- High likelihood that cardiac symptoms following COVID-19 vaccination represent a hypersensitivity eosinophilic myocarditis
- There are important challenges in communicating this experience
  - Clinicians and vaccine recipients must be alert to recognize the importance of evaluating potential myocarditis symptoms
  - AEFI risk communication has the potential to increase vaccine hesitancy at a critical point in pandemic response
  - COVID-19 infection carries far greater risk of cardiac injury
- Continued surveillance will better define experience with, and risk factors for, myocarditis following COVID-19 vaccination leading to best practices

Questions

BACK-UP SLIDES

Case Characteristics

	April 12 Briefing (n=14)	May 17 Briefing (n=23)	July 12 Briefing All Myocarditis (n=39)	Pericarditis (n=4)
Median Age (yrs)	32 (20-51)	25 (20-51)	24 (15-51)	33 (20-40)
Gender				
Male	100% (14)	100% (23)	90% (35)	2
Female	0	0	10% (4)	2
Race				
White	86% (12)	72% (18)	79% (31)	1
Black	14% (2)	9% (2)	8% (3)	2
Other/UNK	0	13% (3)	13% (5)	1
Viral Illness w/in 30 days?				
No	100% (14)	100% (23)	92% (36)	2
Yes	0	0	5% (2)	2
UNK	0	0	3% (1)	0
Viral Studies (IgM)				
NEG	64% (9)	57% (13)	46% (18)	0
POS	0	0	8% (3)	0
Not Done	36% (5)	43% (10)	46% (18)	4
History of COVID disease?				
No	93% (13)	87% (20)	87% (34)	2
Yes	7% (1)	13% (3)	13% (5)	2
Dose #				
2	93% (13)	87% (20)	87% (34)	1
1	7% (1)	13% (3)	13% (5)	3
Chest Pain Onset interval	44 (12-96)	48 (12-132)	48 (12-336)	60 (12-120)

Case Characteristics

	April 12 Briefing (n=14)	May 17 Briefing (n=23)	July 12 Briefing All Myocarditis (n=39)	Pericarditis (n=4)
COVID test (PCR)				
NEG	86% (12)	83% (19)	72% (28)	0
POS	0	0	0	0
Not Done	18% (2)	17% (4)	28% (11)	4
Troponin Elevated?				
Yes	100% (14)	100% (23)	92% (36)	0
No	0	0	0	4
Not Done	0	0	8% (3)	0
EKG Abnromal?				
Yes	86% (12)	83% (19)	79% (31)	2
No	14% (2)	17% (4)	21% (8)	2
Coronary Imaging Abnormal?				
No	86% (12)	70% (16)	59% (23)	1
Yes	0	0	0	0
Not Done	14% (2)	30% (7)	41% (16)	3
cMRI c/w Myocarditis				
Yes	43% (6)	35% (8)	33% (13)	0
No	0	0	8% (3)	1
Not Done	57% (8)	65% (15)	59% (23)	1
Pending Results	----	----	----	1
Vaccine				
Pfizer	3	30% (7)	41% (16)	0
Moderna	11	70% (16)	59% (23)	2
Janssen	0	0	0	2

Myocarditis Case Definition 2003

Suspect

Dyspnea, palpitations, or chest pain of probable cardiac origin, with either one of the following:

(a) ECG abnormalities beyond normal variants, not documented previously, including:

  i. ST-segment/T-wave abnormalities
  ii. Paroxysmal or sustained atrial or ventricular arrhythmias
  iii. AV nodal conduction delays or intraventricular conduction defects
  iv. Continuous ambulatory ECG monitoring that detects frequent atrial or ventricular ectopy,

OR

(b) Focal or diffuse depressed LV function of indeterminate age identified by an imaging study

Probable

Meets criteria for suspected myocarditis and is in the absence of other likely cause of symptoms.

In addition, meets one of the following:

(a) Elevated cardiac enzymes (Troponin I, Troponin T, or Creatine Kinase-MB),

OR

(b) New onset or increased degree of severity of focal or diffuse depressed LV function by imaging,

OR

(c) Abnormal imaging indicating myocardial inflammation (cardiac MRI with gadolinium, gallium-67 scanning, anti-myosin antibody scanning)

Confirmed

Histopathologic evidence of myocarditis by endomyocardial biopsy or on autopsy.

MMWR 2003;52:492-6, ww.cdc.gov/mmwr/PDF/wk/mm5221.pdf

Myocarditis Case Definition 2021

Condition	Definition	
Acute myocarditis	**Probable case**	**Confirmed case**
	Presence of ≥1 new or worsening of the following clinical symptoms:*	Presence of ≥1 new or worsening of the following clinical symptoms:*
	• chest pain, pressure, or discomfort	• chest pain, pressure, or discomfort
	• dyspnea, shortness of breath, or pain with breathing	• dyspnea, shortness of breath, or pain with breathing
	• palpitations	• palpitations
	• syncope	• syncope
	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms:	OR, infants and children aged <12 years might instead have ≥2 of the following symptoms:
	• irritability	• irritability
	• vomiting	• vomiting
	• poor feeding	• poor feeding
	• tachypnea	• tachypnea
	• lethargy	• lethargy
	AND	AND
	≥1 new finding of	≥1 new finding of
	• troponin level above upper limit of normal (any type of troponin)	• Histopathologic confirmation of myocarditis[†]
	• abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis[§]	
	• abnormal cardiac function or wall motion abnormalities on echocardiogram	• cMRI findings consistent with myocarditis[¶] in the presence of troponin level above upper limit of normal (any type of troponin)
	• cMRI findings consistent with myocarditis[¶]	
	AND	AND
	• No other identifiable cause of the symptoms and findings	• No other identifiable cause of the symptoms and findings